

Applicants : Seetharama A. Acharya and Belur N. Manjula  
Appn. No. : 10/538,976  
Filing Date : December 5, 2005  
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#### REMARKS

Claims 8-21 and 28 were pending in the subject application. By this amendment, Claim 28 has been canceled without prejudice or disclaimer, and Claim 8 has been amended. Applicants maintain that the claim amendments do not raise an issue of new matter. Support for the claim amendments can be found at least in the previous version of the claims. Entry of the amendments is respectfully requested.

#### Objections to the Claims

Claim 28, which was objected to, has been canceled thereby rendering this objection moot.

#### Rejections under 35 U.S.C. §102(b)

Claims 8-21 and 28 are rejected as anticipated by Acharya et al. (U.S. Patent No. 6,017,943) (hereinafter "the '943 patent").

Applicants respectfully traverse this rejection.

The '943 patent does not set forth the process recited in Claim 8 for preparing a hemoglobin molecule (Hb) modified to have six  $\pm$  one polyethylene glycol (PEG) chains, comprising the steps of:

- (a) reacting Hb with 8-15 fold excess of iminothiolane to form thiolated Hb; and
- (b) reacting the thiolated Hb with 16-30 fold excess of PEG functionalized with a maleimide moiety, to form the modified Hb having six  $\pm$  one PEG chains.

In particular, the '943 patent does not teach a method for preparing a hemoglobin molecule (Hb) modified to have six  $\pm$  one PEG chains and the '943 patent does not teach reacting a thiolated Hb with 16-30 fold excess of PEG.

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On page 4 of the Office Action, the Examiner carries out some mathematical manipulations, picking and choosing values from among those in the specification of the '943 patent, to allege that the '943 patent teaches using a 2-66 fold excess of PEG over thiolated Hb. Applicants respectfully submit that the Examiner has taken these values out of context, ignoring both the overall teachings of the '943 patent and in particular the section of the '943 patent from which the values were obtained. Rather, the '943 patent teaches the values set forth below.

Example 9 (Column 11) of the '943 patent describes thiolating Hb using a five-fold molar excess of iminothiolane and then adding a two-fold excess of Mal PEG 5000.

The '943 patent teaches that it is preferred that the compound (Ic) be present in about a two-fold molar excess over the hemoglobin concentration (Column 5, lines 51-53). The '943 patent also teaches (Col. 5, line 53 - Col. 6, line 2) that "[t]he concentration of Hb is typically about 0.1 mM to about 3.0 mM, and most preferably about 0.5 mM; the concentration of the compound is typically about 0.2 M to about 6.0 mM, and most preferably about 1.0 mM" which tracks the preferred two-fold molar excess of compound to Hb.

In column 7, lines 8-13, the '943 patent teaches another example with compound (Ic) where "[t]ypical concentrations of Hb range from about 1.5 mM to about 3.0 mM, and preferably about 2.5 mM; for the compound, about 3.0 mM to about 6.0 mM, and preferably about 5.0 mM" again following the preferred two-fold molar excess ratio.

In column 7, lines 50-56, the '943 patent teaches a different example (compound Id) where "[i]t is preferred that the compound is present in about a 2.5-fold molar excess over the Hb concentration. The concentration of Hb is typically about 0.1 mM to about 3.0 mM, and most preferably about 0.5 mM; the concentration of the compound is typically about

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0.25 mM to about 7.5 mM, and most preferably about 1.25 mM” which tracks the 2.5-fold molar excess ratio.

In column 7, line 64 - Column 8, line 17, the ‘943 patent teaches “The hemoglobin composition ... may be prepared by (a) reacting Hb with a thiolating agent such as iminothiolane, and (b) reacting the thiolated Hb with the compound having the formula... (Id) ... For thiolation, concentration of Hb is typically about 0.1 mM to about 3.0 mM, and most preferably about 0.5 mM; the concentration of the thiolating agent is about 5 to 20 fold molar excess over the concentration of Hb... The compound is then added to the reaction mixture preferably at about a 2-fold molar excess over the Hb concentration. Typical concentrations are about 0.2 mM to about 6.0 mM, and most preferably about 1.0 mM” which once again tracks the preferred two-fold molar excess of compound to Hb.

Accordingly, the ‘943 patent does not anticipate the claimed invention. Nor is it obvious from the ‘943 patent that the claimed process would produce a PEGylated Hb having the claimed six  $\pm$  one PEG chains, where in addition the PEGylated Hb produced by the claimed method has advantageous, non-hypertensive properties.

Reconsideration and withdrawal of this rejection are respectfully requested.

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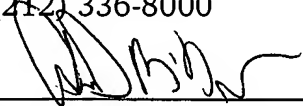
CONCLUSIONS

In view of the amendments and remarks made hereinabove, reconsideration and withdrawal of the objection and rejection set forth in the February 7, 2008 Office Action and passage of the pending claims to allowance are respectfully requested. If there is any minor matter preventing the allowance of the subject application, the Examiner is requested to telephone the undersigned attorney.

No fee is deemed necessary in connection with the submission of this reply. However, if any fee is required to maintain the pendency of the subject application, authorization is hereby given to withdraw the amount of any such fee from Deposit Account No. 01-1785.

Respectfully submitted,  
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New York, New York

By   
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